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EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/525,020	YAMAMOTO ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-22* is/are pending in the application.

4a) Of the above claim(s) *19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-18 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

1. Claims 1-13 have been canceled as filed on 6/13/2005.

Claim 22 has been added as filed on 10/31/06.

Claims 14-22 are currently pending as filed on 10/31/2006.

Claims 19-21 have been withdrawn as previously acknowledged.

Claims 14-18 and 22 are being examined in this application.

Election/Restrictions

2. Applicant's election with traverse of Group 1 (Claims 14-18) over the telephone has been previously acknowledged (see the previous Office action, mailed 3/13/06, pp. 4-5).

Applicant's traversed of the Restriction Requirement over the phone as reflected by the Examiner Interview Summary (mailed 3/13/06). Applicants also filed an Interview Summary of record, filed 7/12/06, which states applicant's traversal over the Restriction Requirement. As discussed in the previous Office action (mailed 3/13/06, pp. 4-5), applicant's argument is not found persuasive.

The traversal is on the ground(s) that the cited prior art does not teach the technical feature for Group 1. This is not found persuasive because the technical feature of Group 1 does not constitute as a special technical feature as defined by PCT Rule 13.2. The different groups of invention do not share a common special technical feature as discussed above. In addition, the assumed linking technical feature of Group 1 claims is a cell comprising a cargo receptor, which

is known in the prior art. Ueno et al (Nihon Yakugakkai Dai 121 nenkai Yoshishu, Page 7; Issued on March 5, 2001; Abstract for a meeting of the Pharmaceutical Society of Japan) teach cells expressing cargo receptor with mutations in the carbohydrate binding domain.

The requirement is still deemed proper and is therefore made FINAL.

3. This application contains claims 19-21 are drawn to an invention nonelected with traverse in the Reply, filed 7/12/06 (p. 6). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

4. Applicants states in the Reply, filed 7/12/06, p. 6, para 5, that "Applicants subsequently filed a reply on March 2, 2006 to include the substance of the interview". However, no such reply is found in the record corresponding to the said date of "March 2, 2006". An "Interview Summary" from the Applicant's representative was filed on 7/12/06.

5. Applicants elected with traverse of the following species as previously acknowledged (Office action, mailed 3/13/06, p.5):

A.) ERGIC-53;

B.) membrane bound protein.

6. Applicant's election of the species "D-Gal" in the reply filed on 10/31/06 is acknowledged. Because applicant did not distinctly and specifically point out the supposed

errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Accordingly, the non-elected species are withdrawn from each corresponding claim.

Priority

7. Applicant's filing of a translation (filed on 7/12/06) for the Foreign application: JAPAN 2002-238559; filed on 8/19/2002) is acknowledged.

Drawings

8. In light of applicant's amendments to the specification (filed 7/12/06) to recited Sequence Identifiers for the sequences in the drawing, the objection to the Drawings is withdrawn.

Sequence Rule Compliance

9. Applicant's filing of a Sequence Listing on 7/12/06 is acknowledged.

Specification

10. In light of applicant's amendments to the specification (filed 7/12/06) to delete the embedded hyperlink, the objection to the specification is withdrawn.

Claim Rejections Withdrawn

11. In light of applicant's argument (Reply, 7/12/06, p. 9, para 2+), and amendment to the claims, the following rejection is withdrawn:

Claims 14-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

However, new claim rejections under 35 U.S.C. 112, second paragraph, are formulated below as necessitated by applicant's amendments to the claims.

12. The following claim rejections have been overcome by the Declarations filed under 37 C.F.R. § 1.132 (7/12/06) by co-inventors, Akira Sato and Junko Shimauchi:

A.) Claims 14-18 are rejected under **35 U.S.C. 102(a)** as being anticipated by Sato (Summary of Master's Thesis, Graduate School of Frontier Science, Dept. of Integrated Biosciences, The University of Tokyo, Page 22-23; 2/18/2002).

B.) Claims 14-18 are rejected under **35 U.S.C. 102(a)** as being anticipated by Shimauchi (Summary of Master's Thesis, Graduate School of Frontier Science, Dept. of Integrated Biosciences, The University of Tokyo, Page 3-7; 2/18/2002).

13. In light of applicants argument (Reply, p. 11, para 4), the following rejection is withdrawn:

A.) Claims 14, 16-18, and 22 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Itin et al (Molecular Biology of the Cell. Vol. 7: 483-493; March 1996; cited previously).

Claim Rejections Maintained

Claim Rejections - 35 USC § 112

14. The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description Rejection

15. Claims 14-18 and 22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection over Claims 14-18 is maintained for the reasons of record as set forth in the Office action, mailed 3/13/06, at pp. 8+. The rejection over Claim 22 is necessitated by applicant's amendment to the claims.

Discussion and Answer to Argument

16. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the specification, especially Examples 1 and 2, "illustrates a variety of heterologous cargo receptors". Thus, the "specification fully supports the present recitation of a plurality of eukaryotic cells, comprising heterologous DNA coding for a variety of

modified cargo receptors, per Claim 17." (Reply, 7/12/06, pp. 7-8, bridging para). Applicants also pointed to recitations of the instant specification to demonstrate supports for the claimed invention (Reply, p. 8, para 3).

The instant claims are drawn to a genus of "eukaryotice cells", which comprise a genus of "DNA" that code for a genus of "cargo receptor". As discussed in the previous Office action (mailed 3/13/06), to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. (See MPEP 2163 II).

Given that the instant specification recites examples that illustrate certain "cargo receptors" in certain cells, the instant specification does not provide neither representative numbers of species for the claimed genuses, nor common core structural and/or functional limitation to show possession of the claimed genuses.

As stated by the applicants, "The present invention, however, is not limited to a particular glycoprotein from which the carbohydrate moiety could be modified". That is to say that the instant invention as claimed can comprise any glycoprotein and/or any carbohydrate moiety. However, as discussed above, the instant specification does not demonstrate the possession of such claimed genuses.

In addition, applicants also does not provide evidence to indicate that all possible "eukaryotic cells" comprising all possible "DNA" encoding all possible "cargo receptors" are

known, or that representative number species of such products are known, or that a common core structure and/or function is know for such products.

Applicants also states "Thus, the present invention is limited neither to modifying a particular carbohydrate moiety of a certain glycoprotein nor to the use a given carbohydrate moiety. Rather, the invention provides eukaryotic cells with modified cargo receptors as a tool for generating a variety of glycoproteins, the carbohydrate moiety of which is altered".

Contrary to applicant's assertion, the "Written Description Rejection" as set forth in the previous Office action (mailed 3/13/06) is not a rejection over the method of using the carbohydrate moiety or the method of making such as moiety. The "Written Description Rejection" is over the claimed product of "a eukaryotic cell" or "a plurality of eukaryotic cells" that comprise "heterologous DNA coding for a cargo receptor ..." (e.g. instant Claim 14).

Furthermore, applicant's statement of "the invention provides eukaryotic cells with modified cargo receptors as a tool for generating a variety of glycoproteins, the carbohydrate moiety of which is altered", recites features that are not claimed.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., "eukaryotic cells with modified cargo receptors as a tool for generating a variety of glycoproteins, the carbohydrate moiety of which is altered") are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants asserts that "As it is well known in the art, however, "cargo receptor" means a type of receptor that is involved in transporting proteins, including glycoproteins, into a cell. By definition, "glycoprotein" connotes a group of conjugated proteins, each containing a carbohydrate as the non-protein component." (Reply, p. 8, para 5).

However, Applicants have not provided any evidence to indicate the fact that the structures and/or functions for all possible "cargo receptors" and/or "glycoproteins" are "well known in the art". Applicants have not demonstrated any common core structure and/or function for the claimed genus of "eukaryotice cells" comprising "DNA" encoding for a genus of "cargo receptors" and/or "glycoproteins". Furthermore, the instant specification provides a definition for the term "cargo receptor" as "a general nomenclature for animal lectins playing important roles in quality control and sorting of glycoproteins" (p. 6, lines 12+ of the spec.), and "the term "cargo receptor" in the present invention is not specifically limited, as long as it recognizes sugar chains (carbohydrate moieties) attached on glycoproteins and is involved in the transport of glycoproteins required in vivo." (p. 7, lines 23+ of the spec.).

Thus, by the definition provided in the instant specification, the term "cargo receptor" can broadly refer to any lectins that are involved in the controlling and sorting glycoproteins.

Applicant's further states "As the foregoing paragraph explains, the present invention does not relate to a particular cargo receptor or a particular glycoprotein, but to an inventive concept of modifying the carbohydrate moiety of a glycoprotein by alteration of a cargo receptor". (Emphasis added; Reply, pp. 8-9, bridging para).

Contrary to applicant's assertion, the instant claims are drawn to a product of either "a eukaryotic cell" (e.g. Claim 14) or "a plurality of eukaryotic cells" (e.g. Claim 17), but not to "an inventive concept" as asserted by applicants. Furthermore, "an inventive concept" is not a statutory patentable subject matter under 35 U.S.C. 101. (see MPEP 2106 IV).

35 U.S.C. 112, second paragraph

17. The following is a quotation of the **second paragraph** of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 14-18 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The rejection over Claims 14-18 and 22 is necessitated by applicant's amendment to the claims as well as applicant's statements of record in the Reply, filed on 7/12/06.

Claim 14 as amended recites the phrase "a cargo receptor that is characterized by an alteration of at least one amino acid in its carbohydrate recognition domain" (emphasis added). It is not clear to which entity the term "its" is referring.

Claim 14-18 and 22 recite the term "cargo receptor" that is comprised by the claimed product of "a eukaryotic cell". The instant specification provides a definition for the term "cargo receptor" as "a general nomenclature for animal lectins playing important roles in quality control and sorting of glycoproteins" (p. 6, lines 12+ of the spec.), and "the term "cargo receptor" in the present invention is not specifically limited, as long as it recognizes sugar chains (carbohydrate

moieties) attached on glycoproteins and is involved in the transport of glycoproteins required in vivo." (p. 7, lines 23+ of the spec.; emphasis added).

However, applicants assert "the chimeric proteins disclosed by the publications cannot function as a cargo receptor. This is so because neither MAH nor BPA lectin can dissociate from the carbohydrate after binding to the latter. The chimeric proteins of the publications localize in the Golgi and do not have mobility in the cell." (Reply, 7/12/06, p. 10, para 4; Emphasis added). This statement from applicants indicate that a lectin that is capable of binding to carbohydrates and localizing (or transporting) the glycoprotein within a cell would not be considered as a "cargo receptor", which is contrary to the definition provided in the instant specification. Thus, one of ordinary skill in the art would not define what is encompassed by the term "cargo receptor" as claimed in the instant application.

Discussion and Answer to Argument

19. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants assert that the claim amendment has overcome the rejection.

However, applicant's amendment to the claims have necessitated new rejection to the claims as discussed above.

Claim Rejections - 35 USC § 102

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

21. Claims 14, and 16-18 are rejected under **35 U.S.C. 102(b)** as being anticipated by Ueno et al (Nihon Yakugakkai Dai 121 nenkai Yoshishu, Page 9; Issued on March 5, 2001; Abstract for a meeting of the Pharmaceutical Society of Japan; Cited in IDS). The previous rejection is maintained for the reasons of record as set forth in the Office action, mailed 3/12/06, at p. 15+. The rejection over Claim 22 is necessitated by applicant's amendment to the claims.

The instant claims recites a eukaryotic cell comprising heterologous DNA coding for a cargo receptor that is characterized by an alteration of at least one amino acid in its carbohydrate recognition domain, such that said cell expresses a glycoprotein with a modified carbohydrate moiety.

Ueno et al teach generation of eukaryotic cells (mammalian cells) comprising ERGIC-53 with altered lectin domains (carbohydrate binding domains). (See the entire abstract) The reference teaches the ERGIC-53 cDNA was altered at its lectin domain (reads on alteration of its carbohydrate recognition domain). (See 2nd paragraph of the reference.) The reference further teaches the said ERGIC-53 cDNA was inserted into a plasmid and expressed in mammalian cells (reads on eukaryotic cell comprising heterologous DNA coding for a cargo receptor). (See 2nd paragraph) The reference also teaches that various alterations to the lectin domain were created

and that "various recombinants ERGIC-53" were transfected into mammalian cells to "obtain various cell lines" (2nd paragraph), which reads on a plurality of eukaryotic cells expressing a variety of carbohydrate recognition domains. The reference further teaches that "a glycoprotein having distinctive glycoform was observed in some of the recombinants ERGIC-53" (see 3rd paragraph), which reads on eukaryotic cells expressing glycoprotein with a particular glycoform.

The reference also teaches BPA lectin binds to galactose (para 2), which reads on the glycofrom (D-Gal) of instant Claim 22). Furthermore, the recitations of "wherein said plurality is enriched for eukaryotic cells that express glycoprotein characterized by a particular glycoform" (the instant Claim 18), and "where in the glycoform comprises at least one selected from the group consisting of D-Gal ..." (Claim 22) are construed as intended use of the claimed product. As discussed above, the eukaryotic cell comprising the cargo receptor is structurally the same as the claimed product, and thus, the cargo receptor taught by the reference is capable of performing the intended function of binding to D-Gal glycoform.

In addition, the eukaryotic cells also inherently comprise glycoproteins with D-Gal glycoform, as evidenced by the instant specification. The instant specification states that the eukaryotic cells are transfected with DNA encoding for mutant "cargo receptors" such as ERGIC-53 mutants, and then isolate cells based on glycoproteins with particular glycoforms (see Examples 1-11, especially, Example 10 of the instant spec.). That is the eukaryotic cells inherently possess glycoproteins with different glycoforms such as D-Gal. For example, Table 5, for example, shows the different glycoforms (including D-Gal) comprised by the eukaryotic cells.

Discussion and Answer to Argument

22. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that because the instant claims (Claim 14) recite that the "cargo receptor" "is altered by at least one amino acid mutation in its carbohydrate recognition domain", the reference's teaching of "the lectin domain of ERGIC-53 or VIP36 is ***entirely replaced*** *by MAH or BPA lectin" does not anticipate the claimed product. (Emphasis provided by applicants; Reply, p. 10, para 3).*

As stated by the applicant's the instant claims recite "alteration of at least one amino acid in its carbohydrate recognition domain", which broadly encompasses mutations of the entire lectin domain. The instant specification defines the terms "alteration of a carbohydrate recognition domain" and "modified carbohydrate moiety" as the followings:

> "the term "alteration of a carbohydrate recognition domain" means that when a cargo receptor is expressed as proteins, its carbohydrate recognition domain or its carbohydrate-binding domain differs from that of native one in terms of sequence and/or structure; or that a carbohydrate moiety (sugar chain) to be added differs from that of native protein to be expressed in cells. Hence, in addition to the above described specific sequences, alteration of a cargo receptor, whereby a carbohydrate moiety differing from that to be added before alteration, is also encompassed in the term "alteration of a carbohydrate recognition domain" according to the present invention." (p. 9, lines 10+ of the spec.).
>
> "the term "modified carbohydrate moiety" or "modified carbohydrate structure" indicates that the sequence and/or the structure of such a carbohydrate moiety differs from that of an unaltered cargo receptor." (p. 20, lines 14+ of the spec.)

The terms as defined by the instant specification, and as recited in the instant claims broadly encompass any alteration of the lectin domain including the entire domain. Furthermore,

the cited reference Ueno et al does not necessarily teach replacement of the entire lectin domain. The Ueno reference teaches "the lectin domain of ERGIC-53 was recombined with that of a sialic acid-binding MAH lectin ..." (para 2 of Ueno), which means parts of the ERGIC-53 and parts of the other lectin domains comprised the final product.

Applicants further argue that "the chimeric proteins disclosed by the publications cannot function as a cargo receptor. This is so because neither MAH nor BPA lectin can dissociate from the carbohydrate after binding to the latter. The chimeric proteins of the publications localize in the Golgi and do not have mobility in the cell." (Reply, 7/12/06, p. 10, para 4; Emphasis added).

Applicants have made the above assertion without any supporting evidence to indicate the fact. Applicants have not provide any evidence to show that "neither MAH nor BPA lectin can dissociate from the carbohydrate after binding to the latter" as well as "the chimeric proteins of the publications localize in the Golgi and do not have mobility in the cell". Even if the above assertion is true, applicants have not shown how these alleged properties of the "cargo receptor" of the reference's teaching differ from the "cargo receptor" as broadly defined by the instant specification (p. 6, lines 12+ of the spec. and p. 7, lines 23+ of the spec.).

Contrary to applicant's assertion, the reference's teaching anticipates the claimed invention of a product that is a eukaryotic cell comprising a "cargo receptor", as broadly defined in the instant specification:

For example, "the term "cargo receptor" in the present invention is not specifically limited, as long as it recognizes sugar chains (carbohydrate moieties) attached on glycoproteins

and is involved in the transport of glycoproteins required in vivo." (p. 7, lines 23+ of the spec.; emphasis added).

Thus, the only required structural and/or functional elements for the claimed "cargo receptor" is "recognizes carbohydrate moieties:, and "transport of glycoproteins". The Ueno reference teaches ERGIC-53 "recognizes mannose" (which mannose is a "carbohydrate moiety), and it is involved in "transport and sorting of proteins" from ER to the Golgi apparatus (para 1 of the reference). The reference also teaches both MAH lectin and BPA lectin bind to carbohydrate moiety (para 2 of the reference). Furthermore, the reference teaches "a glycoprotein having the distinctive glycoform was observed in some of the recombinant ERGIC-53" (para 3). That is the "recombinant ERGIC-53" bind to a glycoform, which is referring to a carbohydrate moiety on a glycoprotein (see p. 8, lines 10+ of the spec. for definition of glycoform). Thus, not only does the components of the final "cargo receptor" of the reference bind to "carbohydrate moieties, but the final recombinant "cargo receptor" (i.e. recombinant ERGIC-53) also bind "carbohydrate moieties".

The reference also teaches that transport signal sequences were used to localize the recombinant "cargo receptor" in ER and trans-Golgi apparatus, and intracellular localization of the recombinant ERCIC-53 with bound glycoproteins was observed (para 2-4), which reads on the transporting function of the "cargo receptor". Applicants assert "The chimeric proteins of the publications localize in the Golgi and do not have mobility in the cell." (Reply, p. 10, para 4). Contrary to applicant's assertion, "localization" does not equal to lack of "mobility", and/or inability to "transport" or "sort" glycoproteins in the cell. ERGIC-53 is known in the art to be "localized" in ER and Golgi apparatus while facilitating "transporting" or "sorting"

glycoproteins in the ER and Golgi apparatus. (see Hauri et al. Journal of Cell Science. Vol. 113: 587-596. 2000; cited in IDS).

Therefore, the recombinant ERGIC-53 is a "cargo receptor" according to the definition of the instant specification, and thus the reference anticipates the claimed invention.

23. Claims 14-18 and 22 are rejected under **35 U.S.C. 102(b)** as being anticipated by Hirai et al (Nihon Yakugakkai Dai 121 nenkai Yoshishu, Page 7; Issued on March 5, 2001; Abstract for a meeting of the Pharmaceutical Society of Japan; Cited in IDS). The previous rejection over Claims 14-18 is maintained for the reasons of record as set forth in the Office action, mailed 3/12/06, at p. 15+. The rejection over Claim 22 is necessitated by applicant's amendment to the claims.

Hirai et al teach the generation of recombinant VIP36 containing cells (See the entire document). The reference teaches that the lectin domain (carbohydrate binding domain) of VIP36 (cargo receptor) was recombined with BPA lectin and MAH lectin (would read on a variety of carbohydrate recognition domain and alteration of the said domain). The reference also teaches the cells used to express the recombinant VIP36 mutants are MDCK cells (would read on a eukaryotic cells). The reference further teaches observing "the structural and functional changes in sugar chains of glycoproteins to be biosynthesized" in the cells comprising the altered carbohydrate recognition domain (See 1st paragraph), which would read on the intend use of expressing glycoprotein with modified carbohydrate moiety. In addition, the reference teaches that the cells having the different chimeric or recombinant cargo receptor expressed

therein specific types of sugar chains of intracellular and extracellular glycoproteins (See last paragraph), which would read on a plurality of cells expressing glycoprotein with a particular glycoform. Furthermore, the reference teaches the intracellular and extracellular localization of the expressed glycoprotein using FACS analysis, which would read on membrane-bound or secretory protein.

The recitations of "wherein said plurality is enriched for eukaryotic cells that express glycoprotein characterized by a particular glycoform" (the instant Claim 18), and "where in the glycoform comprises at least one selected from the group consisting of D-Gal ..." (Claim 22) are construed as intended use of the claimed product. As discussed above, the eukaryotic cell comprising the cargo receptor is structurally the same as the claimed product, and thus, the cargo receptor taught by the reference is capable of performing the intended function of binding to D-Gal glycoform.

In addition, the eukaryotic cells also inherently comprise glycoproteins with D-Gal glycoform, as evidenced by the instant specification. The instant specification states that the eukaryotic cells are transfected with DNA encoding for mutant "cargo receptors" such as VIP36 mutants, and then isolate cells based on glycoproteins with particular glycoforms (see Examples 1-12, especially, Example 12 of the instant spec.). That is the eukaryotic cells inherently possess glycoproteins with different glycoforms such as D-Gal. For example, Table 5, for example, shows the different glycoforms (including D-Gal) comprised by the eukaryotic cells.

Discussion and Answer to Argument

24. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants have traversed the rejection over the Hirai reference with the same arguments as the Ueno reference.

Applicant's are respectively directed to the above discussion under Ueno for answer to arguments.

New Rejections

Claim Rejections - 35 USC § 112

25. The following is a quotation of the **first paragraph** of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement Rejection

26. Claims 14-18 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making eukaryotic cells comprising certain altered "cargo receptors" and certain glycoproteins with modified carbohydrate moiety, does not reasonably provide enablement for making eukaryotic cells comprising any other altered "cargo receptors" and any other glycoproteins with modified carbohydrate moiety. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This rejection is necessitated by applicant's statements in the Reply, filed on 7/12/06, p. 11, para 4.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. §112, first paragraph, have been described *In re Wands*, 8 USPQ2d 1400(1988). They are:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The predictability or lack thereof in the art
5. The level of skill in the art;
6. The amount of direction or guidance present;
7. The presence or absence of working examples;
8. The quantity of experimentation needed.

The breadth of the claims / The nature of the invention

The breadth of the claims seems to encompass any eukaryotic cells comprising any "cargo receptor" having altered carbohydrate recognition domain and any glycoprotein with a modified carbohydrate moiety. No structural and/or functional limitations are provided for the claimed genus of eukaryotic cells, "cargo receptor", and "glycoprotein". The instant specification also does not provide representative number of species for the claimed genuses.

The state of the prior art/ The predictability or lack thereof in the art

The art also does not provide a common core structure for a "cargo receptor" having carbohydrate binding, transporting, and sorting abilities, as defined by the instant specification (p. 6, lines 11+, and p. 7, lines 23+). Furthermore, the art also do not provide a common core structure for "cargo receptor" with altered carbohydrate recognition domain. As stated by applicants (Reply, p. 11, para 4), certain ERGIC-53 mutants have no carbohydrate binding activity, as taught by Itin et al (cited previously in Office action, filed 3/12/06). The Itin reference teaches certain mutations of the wild-type ERGIC-53 (a cargo receptor) eliminated carbohydrate binding (p. 488, left col., para 1). Thus, said mutants of ERGIC-53 would not be "cargo receptors" as defined by the instant specification, because the required carbohydrate binding property is eliminated by the structural change of the protein.

The level of one of ordinary skill

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction or guidance present / The presence or absence of working examples

The only guidance present in the instant specification is directed to certain mutations of ERGIC-53 and VIP36 cargo receptors (see Examples of the instant specification). There is no guidance described for generating any other cells comprising any other mutants of any other cargo receptors. The instant specification does not provide guidance for the structural requirements (such as amino acid core sequence or protein core structure) of a cargo receptor with altered carbohydrate recognition domain. More specifically, the instant specification does

not provide any guidance on what "alterations" of the carbohydrate recognition domain would still possess carbohydrate binding ability as required by a "cargo receptor", as defined by the instant specification.

The quantity of experimentation needed

Due to the unpredictabilities of making a "cargo receptor" with altered carbohydrate recognition binding domain that is comprised by a eukaryotic cell, undue experimentation would be required. The art has not demonstrated all the possible "cargo receptor", and all the possible alterations of the carbohydrate recognition domain. The art has not demonstrated that all mutants of cargo receptors can be successfully expressed in cells and would possess the desired carbohydrate binding, and glycoprotein transporting activity. Because the instant specification only provides guidance for two cargo receptors with limited number of mutations, undue experimentation would be required to practice claimed product.

Conclusion

Due to the non-routine experimentation necessary to determine the suitable mutations for cargo receptors; the lack of direction/guidance presented in the specification regarding the specific requirements for product; the unpredictability of making a successful "cargo receptor" with alterations in the carbohydrate recognition domain as established by the state of the prior art; the breadth of the claims, undue experimentation would be required of a skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SL
Art Unit 1639
2/19/2007

JON EPPERSON
PRIMARY EXAMINER